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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
LU, FRANK WEI MIN	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 06/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/760,819	STANLEY, CHRISTOPHER J.	
	Examiner	Art Unit	
	Frank W Lu	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 March 2006* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-18,20,23-26 and 28-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-18,20,23-26 and 28-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 January 2001 (original)* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. *09/313,385* .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

CONTINUED EXAMINATION UNDER 37 CFR 1.114 AFTER FINAL REJECTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission of RCE, the amendments and declaration under 37 CFR § 1.132 filed on March 29, 2006 have been entered. The claims pending in this application are claims 1, 3-18, 20, 23-26, and 28-34. Rejection and/or objection not reiterated from the previous office action are hereby withdrawn in view of amendment filed on March 29, 2006.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Scope of Enablement

Claims 1, 3-17, 20, 23-26, and 28-34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for performing the methods recited in 1, 3-17, 20, 23-26, and 28-34 when said carrier macromolecule is a homopolyamino acid or dextran, does not reasonably provide enablement for performing the methods recited in 1, 3-17, 20, 23-26, and 28-34 when said carrier macromolecule is amylase or pectin or natural gum. The specification does

not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In *In re Wands*, 858 F.2d 731,737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) the court considered the issue of enablement in molecular biology. The Court summarized eight factors to be considered in a determination of "undue experimentation". These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims. The Court also stated that although the level of skill in molecular biology is high, results of experiments in molecular biology are unpredictable.

To begin, there is no direction or guidance in the specification to show that the methods recited in 1, 3-17, 20, 23-26, and 28-34 can be performed when said carrier macromolecule is amylase or pectin or natural gum. While the relative skill in the art is very high (the Ph.D. degree with laboratory experience), there is no predictability whether the methods recited in 1, 3-17, 20, 23-26, and 28-34 can be performed when said carrier macromolecule is amylase or pectin or natural gum.

Claims 1, 3-17, 20, 23-26, and 28-34 are directed to a process for the amplification of a nucleic acid template wherein said carrier macromolecule is amylase or pectin or a natural gum. Since the specification does not provide a guidance to show how a nucleic acid is labeled with amylase or pectin or a natural gum and art search cannot locate references related to a method for labeling a nucleic acid with amylase or pectin or a natural gum. In view of claims 1, 3-17, 20,

23-26, and 28-34, it is unclear how a nucleic acid can be labeled with amylase or pectin or a natural gum so that the methods recited in 1, 3-17, 20, 23-26, and 28-34 can be performed.

With above unpredictable factor, the skilled artisan will have no way to predict the experimental results. Accordingly, it is concluded that undue experimentation is required to make the invention as it is claimed. The undue experimentation at least includes to test whether a nucleic acid can be labeled with amylase or pectin or a natural gum.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Campbell (US H1398, published on January 3, 1995) in view of Yamane *et al.*, (US Patent No. 4,876,335, published on October 24, 1989).

Regarding claim 1, Campbell teaches providing a primer, hybridizing the bound primer to said template (ie., the target DNA from the crude preparation); and extending said primer to form an extended primer (ie., amplified product) and performing amplification of the nucleic acid template as recited in the claim.

Campbell does not disclose that a primer covalently bound to a non-nucleotide carrier macromolecule wherein said carrier macromolecule is water soluble at a temperature in the range of 0-60°C such as a homopolyamino acid as recited in claim 1.

Yamane *et al.,* teach that a polylysine-labeled oligonucleotide is used as a probe or a primer and lysine residues on the polylysine can be any desired numbers wherein the polylysine is covalently connected to the oligonucleotide (see column 2). Since polylysine is water soluble at a temperature in the range of 0-60°C (see attachment for lysine and polylysine), polylysine is said carrier macromolecule as recited in claim 1.

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed the method recited in claim 1 wherein a primer covalently bound to a non-nucleotide carrier macromolecule and said carrier macromolecule is water soluble at a temperature in the range of 0-60°C and is homopolyamino acid (ie., polylysine) in view of the prior art of Campbell and Yamane *et al.*. One having ordinary skill in the art would have been motivated to do so because Yamane *et al.,* teach advantages for using polylysine-labeled oligonucleotide as a probe or a primer "a. Since no labeling substance is contained in the base moiety of nucleotide, substantially no change occurs in the melting point (Tm value), and it is stable. b. Synthesis of a poly-labeled oligonucleotide having any base sequence is possible. c. Synthesis is easy and synthesis of a large amount is possible. d. Since a plurality of labeling substances are bound, the detection sensitivity is good.

e. It can be used as a primer (fragment complementary to DNA) necessary for base sequence determination of DNA according to the Sanger method" (see column 2) and the simple replacement of one kind of primer (ie., the primer taught by Campbell) from another kind of primer (i.e., polylysine-labeled oligonucleotide primer taught by Yamane *et al.,*) during the process for making a primer recited in claim 1 would have been, in the absence of convincing evidence to the contrary, *prima facie* obvious to one having ordinary skill in the art at the time

the invention was made since the primer taught by Campbell and the primer taught by Yamane *et al.,* are used for the same purpose (ie., working a primer) and are exchangeable.

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.06, 2144.07 and 2144.09.

Also note that there is no invention involved in combining old elements is such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. In re Rose 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

6. Claims 3-5, 7-9, 11-13, 23-26, 28, 30, and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Campbell in view of Gold *et al.,* (US Patent No. 6,011,020, filed on May 4, 1995).

Regarding claim 3, Campbell teach providing a primer, hybridizing the bound primer to said template (ie., the target DNA from the crude preparation), and extending said primer to form an extended primer (ie., amplified product) which replicates from said template as recited in the claim.

Regarding claim 23, Campbell teaches providing a primer, hybridizing the bound primer to said template (ie., the target DNA from the crude preparation), and extending said primer to form an extended primer (ie., amplified product) which replicates from said template as recited in the claim.

Regarding claims 8, 9, 11, 13, 28, and 30, since Campbell teaches that said primer is extended by a polymerase wherein said polymerase incorporates nucleotides into said primer wherein said primer is extended in a polymerase chain amplification and said template is a double stranded template and is denatured to a single stranded form, said carrier macromolecule-bound primer is complementary in sequence to a region of one of the template strands and a second primer is provided which is complementary in sequence to a region of the other strand, which second primer is also extended so as to form a complementary sequence copy of said template second strand as recited in claims 8, 9, 11, 28, and 30 (see columns 2 and 3). Since claim 13 does not limit that "carrier macromolecule" is a non-nucleotide carrier macromolecule recited in claim 3 and Campbell teaches a primer having a site for double stranded DNA binding protein in its 5' end (see column 3), Campbell discloses a second primer with a carrier macromolecule (ie., a double stranded DNA binding protein) as recited in claims 13.

Campbell does not disclose a primer covalently bound to a carrier macromolecule via one or more moieties derived from divinyl sulfone wherein the carrier macromolecule is dextran or dextran derivative as recited in claims 3, 7, and 24 and said carrier macromolecule such as dextran is bound to solid support as recited in claims 12 and 31.

Gold *et al.,* teach a nucleic acid covalently bound to a carrier macromolecule (ie., dextran) via one or more moieties derived from divinyl sulfone as recited in claims 3, 7 ,23, and 24 (see column 8, fourth paragraph and column 18, second paragraph).

Regarding claims 4, 5, and 24-26, since it is known that dextran is a linear polysaccharide made of many glucose molecules joined into a long chain and dextran/salt solutions are sometimes used to replace lost blood in emergency situation (see attachment for dextran in the

office action mailed on May 25, 2005), dextran must be water soluble with pH of 4-10. Thus Gold *et al.,* disclose that the carrier macromolecule (ie., dextran) in its free state is substantially linear and substantially charged at a pH in the range of 4 to 10 as recited in claims 4, 24, and 25. Since dextran taught by Gold *et al.,* is 1000 Da or more (see column 8, lines 45-53), Gold *et al.,* disclose that said non-nucleotide carrier macromolecule or said dextran has a peak molecular weight in the range of 1,000 to 40,000,000 as recited in claims 5 and 26.

Regarding claim 12, since Campbell teaches to attach amplified product on a support (see column 4, second paragraph), Campbell in view of Gold *et al.,* discloses said carrier macromolecule (ie., dextran) is bound to a solid support after the amplification as recited in claim 12.

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed the methods recited in claims 3, 7, and 23 using a primer covalently bound to a carrier macromolecule (ie., dextran) via one or more moieties derived from divinyl sulfone in view of the prior art of Campbell and Gold *et al.*. One having ordinary skill in the art would have been motivated to do so because Gold *et al.,* have successfully made a nucleic acid covalently bound to a carrier macromolecule (ie., dextran) via one or more moieties derived from divinyl sulfone and the simple replacement of one well known label (ie., fluorescent label taught by Campbell, see column 3, last paragraph) from another well known label (i.e., dextran taught by Gold *et al.,*) during the process for making a primer recited in claim 3 or 7 or 23 would have been, in the absence of convincing evidence to the contrary, *prima facie* obvious to one having ordinary skill in the art at the time the invention

was made because both fluorescent label and dextran are used for the same purpose (ie., using as oligonucleotide labels).

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.06, 2144.07 and 2144.09.

Also note that there is no invention involved in combining old elements is such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. In re Rose 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

7. Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Campbell and Gold *et al.,* as applied to claims 3-5, 7-9, 11-13, 23-26, 28, 30, and 31 above, and further in view of Mehta *et al.,* (US Patent No. 5,308,750, published on May 3, 1994).

The teachings of Campbell and Gold *et al.,* have been summarized previously, *supra*.

Campbell and Gold *et al.,* do not disclose that said carrier macromolecule such as dextran has a molecular weight in excess of 80,000 Daltons as recited in claim 6. However, Gold *et al.,* teach that dextran used by them is 1000 Da or more (see column 8, lines 45-53),

Mehta *et al.,* teach that dextran with different molecular weights is commercially available. These dextran includes dextran having a molecular weight in excess of 80,000 Daltons (see column 9).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed the method recited in claim 6 wherein said carrier macromolecule such as dextran has a molecular weight in excess of 80,000 Daltons in view of references of Campbell, Gold *et al.,* and Mehta *et al.*. One having ordinary skill in the art has been motivated to do so because optimization of dextran with different molecular weights during the process for performing the method recited in claim 5, in the absence of convincing evidence to the contrary, would have been obvious to one having ordinary skill in the art at the time the invention was made. One having ordinary skill in the art at the time the invention was made would have been a reasonable expectation of success to perform the method recited in claim 6 using dextran having a molecular weight in excess of 80,000 Daltons. More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. Where the general conditions of a claim are disclosed in the prior art, it is not inventive, in the absence of an unexpected result, to discover the optimum or workable ranges by routine experimentation. *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) (MPEP 2144.05).

8. Claims 10, 14-17, 29, 32, and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Campbell and Gold *et al.,* as applied to claims 3-5, 7-9, 11-13, 23-26, 28, 30, and 31 above, and further in view of Landegren *et al.,* (US Patent No. 4,988,617, published on January 29, 1991).

The teachings of Campbell and Gold *et al.,* have been summarized previously, *supra*.

Campbell and Gold *et al.,* do not disclose that said primer is extended by the action of a ligase ligating said primer to at least one another primer hybridized to said template as recited in claims 10 and 29, said another primer which is ligated by said ligase is also bound to a carrier macromolecule wherein during the extension, a detectable marker is incorporated into one of the extended primers as recited in claims 14 and 15, said extension of one of the primers is conducted *in situ* in a biological sample wherein said biological sample is a plant or animal tissue sample, microorganism culture, or microorganism culture medium as recited in claims 16, 17, 32, and 33.

Landegren *et al.,* teach a ligase chain reaction using two primers with different labels (see Figure 1, column 4, lines 12-50, column 8, lines 43-46, and column 10, last paragraph). Since claim 14 does not limit that "carrier macromolecule" is a non-nucleotide carrier macromolecule recited in claim 3 and biotin on one of the primers taught by Landegren *et al.,* is a carrier molecule and a detectable marker as recited in claims 14 and 15. Therefore, Landegren *et al.,* teach that said primer is extended by the action of a ligase ligating said primer to at least one another primer hybridized to said template as recited in claims 10 and 29, said another primer which is ligated by said ligase is also bound to a carrier macromolecule wherein during the extension, a detectable marker is incorporated into one of the extended primers as recited in claims 14 and 15. Since Landegren *et al.,* teach to use DNA from sickle cell patient for *in situ* analysis, Landegren *et al.,* disclose that said extension of one of the primers is conducted *in situ* in a biological sample wherein said biological sample is an animal tissue sample as recited in claims 16, 17, 32, and 33.

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art

at the time the invention was made to have performed the methods recited in claims 10, 14-17, 29, 32, and 33 in view of the prior art of Campbell, Gold *et al.,* and Landegren *et al.*. One having ordinary skill in the art would have been motivated to do so because Landegren *et al.,* have successfully extended a primer by ligase chain reaction using two primers with different labels and the simple replacement of one well known replication method (i.e., the method taught by Campbell) from another well known replication method (i.e., the method taught by Landegren *et al.,*) during the process of performing the methods recited in claims 10,14-17, 29, 32, and 33 would have been, in the absence of convincing evidence to the contrary, *prima facie* obvious to one having ordinary skill in the art at the time the invention was made because the method taught by Campbell and the method taught by Landegren *et al.,* are functional equivalent methods which are used for the same purpose (ie., extending a primer).

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.06.

9. Claim 20 is rejected under 35 U.S.C. 103(a) as being unpatentable over Campbell, Gold *et al.,* and Landegren *et al.,* as applied to claims 3-5, 7-17, 23-26, and 28-31 above, and further in view of Barany *et al.,* (US Patent NO. 6,027,889, priority date: May 28, 1996).

The teachings of Campbell, Gold *et al.,* and Landegren *et al.,* have been summarized previously, *supra*.

Campbell, Gold *et al.,* and Landegren *et al.,* do not disclose using the probe to detect the nucleic acid sequence in a sample by hybridization thereto as recited in claim 20. However, as shown above, Campbell, Gold *et al.,* and Landegren *et al.,* teach making a probe for detecting said sequence by using said sequence as a template sequence in the method as claimed in claim 17 such that a probe comprises said extended primer that has a sequence complementary to said sequence to be detected is bound to said carrier macromolecule, removing any free nucleic acid not bound to said carrier macromolecule thereof as recited in claim 20.

Barany *et al.,* teach to detect the nucleic acid sequence in a sample by hybridization using the ligated probe (see Figure 1).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed the method recited in claim 20 in view of the prior art of Campbell, Gold *et al.,* Landegren *et al.,* and Barany *et al.*. One having ordinary skill in the art would have been motivated to do so because Barany *et al.,* have successfully used a ligated product as a probe for a hybridization assay (see Figure 1). One having ordinary skill in the art at the time the invention was made would have been a reasonable expectation of success to use a ligated product recited in claim 17 as a probe for a hybridization assay.

10. Claim 34 is rejected under 35 U.S.C. 103(a) as being unpatentable over Campbell in view Gold *et al.,* as applied to claims 3-5, 7-9, 11-13, 23-26, 28, 30, and 31 above, and further in view of Yamane *et al.,* (US Patent No. 4,876,335, published on October 24, 1989).

The teachings of Campbell and Gold *et al.,* have been summarized previously, *supra*.

Campbell and Gold *et al.,* do not disclose that said carrier macromolecule is a

homopolyamino acid. However, Gold *et al.,* teach a nucleic acid covalently bound to a carrier macromolecule (ie., polypeptide) via one or more moieties derived from divinyl sulfone (see column 8, fourth paragraph and column 18, second paragraph).

Yamane *et al.,* teach that a polylysine-labeled oligonucleotide is used as a probe or a primer and lysine residues on the polylysine can be any desired numbers wherein the polylysine is covalently connected to the oligonucleotide (see column 2).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed the method recited in claim 34 wherein the said carrier macromolecule is a homopolyamino acid (ie., polylysine) in view of the prior art of Campbell, Gold *et al.,* and Yamane *et al.*. One having ordinary skill in the art would have been motivated to do so because Gold *et al.,* have successfully made a nucleic acid covalently bound to a carrier macromolecule (ie., polypeptide) via one or more moieties derived from divinyl sulfone, Yamane *et al.,* teach advantages for using polylysine-labeled oligonucleotide as a probe or a primer "a. Since no labeling substance is contained in the base moiety of nucleotide, substantially no change occurs in the melting point (Tm value), and it is stable. b. Synthesis of a poly-labeled oligonucleotide having any base sequence is possible. c. Synthesis is easy and synthesis of a large amount is possible. d. Since a plurality of labeling substances are bound, the detection sensitivity is good. e. It can be used as a primer (fragment complementary to DNA) necessary for base sequence determination of DNA according to the Sanger method" (see column 2) and the simple replacement of one well known label (ie., fluorescent label taught by Campbell, see column 3, last paragraph) from another well known label (i.e., polypeptide such as polylysine taught by Yamane *et al.,*) during the process for making a primer recited in claim 34

would have been, in the absence of convincing evidence to the contrary, *prima facie* obvious to one having ordinary skill in the art at the time the invention was made because both fluorescent label and polypeptide such as polylysine are used for the same purpose (ie., using as oligonucleotide labels).

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.06, 2144.07 and 2144.09.

Also note that there is no invention involved in combining old elements is such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. In re Rose 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

11. Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Steeg *et al.,* (US Patent No. 5,753,437, filed on February 28, 1995) in view of Matteucci *et al.,* (US Patent No. 54,34,257, published on July 18, 1995).

Note that, in this rejection, the phrase "providing a first nucleic acid bound to a non nucleotide carrier macromolecule having a molecular weight in excess of 100,000 Daltons; providing a second nucleic acid bound to a non-nucleotide carrier macromolecule having a molecular weight in excess of 100,000 Daltons" recited in the claim is read as providing a first nucleic acid bound to a non-nucleotide carrier macromolecule wherein the non-nucleotide carrier macromolecule has a molecular weight in excess of 100,000 Daltons and providing a second

nucleic acid bound to a non-nucleotide carrier macromolecule wherein the second nucleic acid has a molecular weight in excess of 100,000 Daltons.

Regarding claim 18, Steeg *et al.,* teach providing a first nucleic acid (NM23 probe labeled with a radiolabel), providing a second nucleic acid bound to a non-nucleotide carrier macromolecule (ie., poly-lysine) wherein the second nucleic acid (ie., nucleic acids from chromosome in tumor cells) has a molecular weight in excess of 100,000 Daltons, contacting said first and second nucleic acids under hybridization conditions, and detecting hybridization between said first and second nucleic acids (see column 17, lines 56-67, and column 18, lines 1-26).

Steeg *et al.,* do not disclose providing a first nucleic acid bound to a non-nucleotide carrier macromolecule wherein the non-nucleotide carrier macromolecule has a molecular weight in excess of 100,000 Daltons.

Since Matteucci *et al.,* teach that different labels such as radiolabel and alkaline phosphatase are used to label a nucleic acid probe (see column 11) and alkaline phosphatase has a molecular weight of 138,000 Da (see attachment for alkaline phosphatase), Matteucci *et al.,* disclose that a non-nucleotide carrier macromolecule (ie., alkaline phosphatase) has a molecular weight in excess of 100,000 Daltons as recited in the claim.

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed the methods recited in claim 18 using a first nucleic acid bound to a non-nucleotide carrier macromolecule wherein the non-nucleotide carrier macromolecule has a molecular weight in excess of 100,000 Daltons (ie., alkaline phosphatase) in view of the prior art of Steeg *et al.,* and Matteucci *et al.*. One having ordinary

skill in the art would have been motivated to do so because Matteucci *et al.*, teach that different labels such as radiolabel and alkaline phosphatase are used to label a nucleic acid probe (see column 11) and the simple replacement of one well known label (ie., radiolabel taught by Steeg *et al.*,) from another well known label (i.e., alkaline phosphatase taught by Matteucci *et al.*,) during the process for making the first nucleic acid recited in claim 18 would have been, in the absence of convincing evidence to the contrary, *prima facie* obvious to one having ordinary skill in the art at the time the invention was made because both radiolabel and alkaline phosphatase are used for the same purpose (ie., using as nucleic acid labels).

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.06, 2144.07 and 2144.09.

Also note that there is no invention involved in combining old elements is such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. In re Rose 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

Conclusion

12. No claim is allowed.

13. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30

(November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is (571)273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (571)272-0746. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571)272-0735.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

June 12, 2006

FRANK LU
PRIMARY EXAMINER